UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,669	08/09/2006	Daniel H.S. Lee	2681.0470001/EJH/SAC	4039

53644 7590 12/10/2009

STERNE, KESSLER, GOLDSTEIN & FOX, P.L.L.C.
1100 NEW YORK AVE., N.W.
WASHINGTON, DC 20005

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,669	LEE ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42 and 44-60* is/are pending in the application.

4a) Of the above claim(s) *48 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,44-47,49-56,58-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final rejection filed on August 17, 2009 is acknowledged.

Claim 43 has been cancelled. Claims 42 and 44-60 are pending in this application. A search was conducted on the elected species, SEQ ID NO: 3, and a prior art was found. Claims 48 and 57 remain withdrawn from further consideration as being drawn to nonelected species. **Claims 42, 44-47, 49-56 and 58-60 are examined on the merits in this office action.**

1. This application contains claims 48 and 57 drawn to an invention nonelected with traverse in the reply filed on June 08, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objections and Rejections

2. Objection to claims 42, 49, 56 and 58 are hereby withdrawn in view of Applicant's amendment to the claims.

3. Claims 50 and 59 rejected under 35 U.S.C. 112, second paragraph are hereby withdrawn in view of Applicant's amendment to the claims.

Maintained Rejection

35 U.S.C. 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 42, 44-47, 49-50, 52-56, 58-59 remain rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al (US 2005/0271655 A1, provisional date August 10, 2002 and published on December 8, 2005, filed with IDS).

6. Lee et al teach SEQ ID NO: 7 which comprises the instant SEQ ID NO: 3. The reference teaches that a soluble Nogo receptor-1 polypeptide consisting essentially of a N-terminal domain (NT), 8 leucine rich repeat domains (LRR) and a LRR C-terminal domain (LRRCT) of Nogo receptor-1...a soluble Nogo receptor-1 polypeptide selected from the group consisting of: amino acid residues 26-344 of SEQ ID NO: 6; **amino acid residues 26-310 of SEQ ID NO: 7**; amino acid residues 26-344 of SEQ ID NO: 8; amino acid residues 26-310 of SEQ ID NO: 9; amino acid residues 27-344 of SEQ ID NO:8; and amino acid residues 27-310 of SEQ ID NO: 9 (see paragraph [0024]), meeting the limitation of claims 49 and 58. The reference teaches a method of promoting survival of a neuron comprising contacting the neuron with an effective

amount of a soluble Nogo receptor-1 polypeptide...the soluble Nogo receptor-1 polypeptide is a fusion protein, e.g., an Fc-fusion protein. In some embodiments, the neuron is in a mammal displaying signs of symptoms of, e.g., multiple sclerosis, ALS, Huntington's disease, **Alzheimer's disease**, Parkinson's disease...spinal cord injury (see paragraph [0021]), meeting the limitations of claims 42-44, 47, 49-50, 52, 56, and 58-59. Furthermore, the reference teaches that dosage regimens may be adjusted to provide the optimum desired response, a single bolus may be administered…to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage unit (see paragraph [0140]. The reference teaches providing a soluble Nogo receptor-1 polypeptide at or near the site of the neurons (see paragraphs [0145] and [0151] and [0153]), meeting the limitation of claims 46 and 55. The instant claims do not define the patient population. The claims are drawn to a method of reducing the symptoms, not treating the disease. Therefore, anybody being administered the soluble Nogo-receptor polypeptide would necessarily have reduction in Aβ peptide levels. Therefore, the reference meets the limitation of claims 42, 44-47, 49-50, 52-56 and 58-59. Please note, the reference also teaches the nonelected species, instant SEQ ID NOS: 4, 5 and 6.

7. Claims 42, 44-47, 49-50, 52-56, 58-59 remain rejected under 35 U.S.C. 102(a) as being anticipated by Lee et al (US 2005/0271655 A1).

8. The teachings of Lee et al are described, *supra*.

Response to Applicant's Arguments

9. Applicant argues that "Applicants have amended claims 42 and 52 to recite that the methods comprise 'administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide' or 'in need of reduction of plaque deposits'." Applicant argues that "Lee does not expressly or inherently disclose the administration of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits."

10. Applicant's arguments have been fully considered but have not been found persuasive. The active method step of the instant claim 42 is "administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide." Claim 44 recites that the "disease, disorder or condition is Alzheimer's disease". The active method step of the instant claim 52 is "administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduction of plaque deposit." Claim 53 recites that the "disease, disorder or condition is Alzheimer's disease". Lee reference explicitly teaches the same active method steps of instant claims. Lee reference teaches a method of administering an effective amount of soluble Nogo receptor-1 polypeptide and Nogo receptor-1 polypeptide fusion protein (Fc-fusion protein) to a mammal displaying signs or symptoms of multiple sclerosis, ALS, Huntington's' disease, Alzheimer's disease, Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injuries and spinal cord injury (see paragraph [0021]). Furthermore, the reference explicitly claims the

method of administering a soluble Nogo receptor-1 polypeptide to the mammal displaying signs or symptoms of MS, ALS, Huntington's disease, Alzheimer's disease, Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injuries or spinal cord injury (see claim 64). The Lee reference teaches the SEQ ID NO: 7 which comprises the instant SEQ ID NO: 3. The reference teaches that a soluble Nogo receptor-1 polypeptide consisting essentially of a N-terminal domain (NT), 8 leucine rich repeat domains (LRR) and a LRR C-terminal domain (LRRCT) of Nogo receptor-1...a soluble Nogo receptor-1 polypeptide selected from the group consisting of: amino acid residues 26-344 of SEQ ID NO: 6; **amino acid residues 26-310 of SEQ ID NO: 7**; amino acid residues 26-344 of SEQ ID NO: 8; amino acid residues 26-310 of SEQ ID NO: 9; amino acid residues 27-344 of SEQ ID NO:8; and amino acid residues 27-310 of SEQ ID NO: 9 (see paragraph [0024]). Lee reference explicitly teaches nine (9) diseases that the Nogo receptor-1 polypeptide and fusion proteins are administered to. Therefore, one of ordinary skill in the art would at once envisage the administration of an Alzheimer's patient with the Nogo receptor-1 polypeptide. The MPEP states the following: When the compound is not specifically named, but instead it is necessary to select potions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated

(See MPEP 2105). Furthermore, since the reference teaches the same active method steps (i.e., same compounds, the same dose and the same patient population), the reference administering Nogo receptor-1 polypeptide to the Alzheimer's patients would inherently reduce levels of Ab peptide or reduce the plaque deposits. Therefore, reference meets the limitation of claims 42, 44-47, 49-50, 52-56, and 58-59.

11. Claims 42, 44-47, 50-56 and 59-60 remain rejected under 35 U.S.C. 102(e) as being anticipated by Strittmatter (US 2002/0077295 A1, filed on October 6, 2001 and published on June 20, 2002, filed with IDS).

12. Strittmatter SM teaches the soluble NgR1 polypeptide having 283 amino acid residues (see SEQ ID NO: 55). This peptide sequence is different from the elected sequence SEQ ID NO: 3 in that it is missing the first proline and the last cysteine residues. Since the sequence has the NT domain, eight leucine rich repeats, and an LRRCT (leucine-rich-repeat domain C-terminal of the eight leucine-rich repeats) domain, this meets the limitation of claims 42 and 52. Strittmatter teaches that the soluble NgR1 polypeptide is used for the treatment of central nervous system disease, disorder or injury, and the term CNS includes, altered CNS function resulting from physical trauma to cerebral or spinal chord tissue, viral infection, autoimmune mechanism, genetic mutation and neurodegenerative diseases or disorders (see paragraph [0084]). The reference further teaches that the typical dosage comprises 1 pg/kg to 100mg/kg body weight, preferred dosage for systemic administration comprise 100 ng/kg to 100 mg/kg; preferred dosages for direct administration to a site via

microinfusion comprise 1 ng/kg to 1 μg/kg body weight (see paragraph [0178]). Since the range of the dosage encompasses the 0.001 mg/kg to 10 mg/kg range, this meets the limitation of claims 51 and 60. Since the neurodegenerative patient population encompasses Alzheimer's disease, the administration of an effective amount of a soluble Nogo receptor-1 polypeptide to neurodegenerative patient would inherently reduce the levels of Aβ peptide and plaque deposition. The reference teaches that administration of the Nogo peptide agents may be transplanted to a site spinal cord injury to facilitate axonal growth throughout the injured site (see paragraph [0173]), meeting the limitation of claims 46 and 55. The reference teaches that the agents can be administered via parenteral, subcutaneous, intravenous, intramuscular, intraperitoneal, transdermal, or bucal routes…an agent may be administered locally to a site of injury via microinfusion. Typical sites include, damaged areas of the spinal cord resulting from injury or damage sites in the brain (see paragraph [0177]), meeting the limitations of claims 45 and 54. As evidenced by instant specification, "bolus injection" is an injection of an aqueous solution (see paragraph [0053 of instant specification). Since the reference teaches the parenteral administration of the Nogo-1 peptide, this reads on claims 45 and 54. The reference teaches 140-AP and AP-Nogo-66 fusion proteins (see paragraph [0061] and Figure 15), meeting the limitation of claims 50 and 59. Therefore, the reference anticipates claims 42, 44-47, 50-56 and 59-60.

13. Claims 42, 44-47, 50-56 and 59-60 remain rejected under 35 U.S.C. 102(a) as being anticipated by Strittmatter (US 2002/0077295 A1).

14. The teachings of Strittmatter are described, *supra*.

Response to Applicant's Arguments

15. Applicant argues that "Applicants have amended claims 42 and 52 to recite that the methods comprise 'administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide' or 'in need of reduction of plaque deposits'." Applicant argues that "claims 42 and 52, as currently presented, do define the patient population, as they are drawn to methods of treating the disease, disorder, or condition comprising administering a therapeutically effective amount of soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits."

16. Applicant's arguments have been fully considered but have not been found persuasive. The active method step of the instant claim 42 is "administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide." Claim 44 recites that the "disease, disorder or condition is Alzheimer's disease". The active method step of the instant claim 52 is "administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduction of plaque deposit." Claim 53 recites that the "disease, disorder or condition is Alzheimer's disease". Strittmatter reference teaches the same active method steps. Strittmatter teaches that the soluble NgR1 polypeptide is used for the treatment of central nervous system disease, disorder or injury, and the term CNS includes, altered CNS function resulting from physical trauma to cerebral or spinal chord tissue, viral infection, autoimmune mechanism, genetic mutation and

neurodegenerative diseases or disorders (see paragraph [0084]). The reference further teaches that the typical dosage comprises 1 pg/kg to 100mg/kg body weight, preferred dosage for systemic administration comprise 100 ng/kg to 100 mg/kg; preferred dosages for direct administration to a site via microinfusion comprise 1 ng/kg to 1 μg/kg body weight (see paragraph [0178]). It is well known in the art that neurodegenerative diseases encompass Alzheimer's diseases, ALS, Huntington's disease, Lewy body disease, Parkinson's disease, Spinal muscular atrophy (see www.nlm.nih.gov/medline/degenerativenervediseases.html, enclosed). The reference explicitly teaches that central nervous system disease, disorder or injury include altered CNS function resulting from physical trauma to cerebral or spinal chord tissue, viral infection, autoimmune mechanism, genetic mutation and neurodegenerative diseases or disorders (5 disorders). Therefore, one of ordinary skill in the art would at once envisage what is encompassed within neurodegenerative diseases. The MPEP states the following: When the compound is not specifically named, but instead it is necessary to select potions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated (See MPEP 2105). Strittmatter reference teaches a Nogo receptor-1 polypeptide sequence that is different from the elected sequence SEQ ID

NO: 3 in that it is missing the first proline and the last cysteine residues. Since the sequence has the NT domain, eight leucine rich repeats, and an LRRCT (leucine-rich-repeat domain C-terminal of the eight leucine-rich repeats) domain, this meets the limitation of claims 42 and 52. Therefore, one of ordinary skill in the art would at once envisage the administration of an Alzheimer's patient with the Nogo receptor-1 polypeptide. Furthermore, since the reference teaches the same active method steps (i.e., same compounds, the same dose and the same patient population), the reference administering Nogo receptor-1 polypeptide to the Alzheimer's patients would inherently reduce levels of Aβ peptide or reduce the plaque deposits. Therefore, reference meets the limitation of claims 42, 44-47, 50-56 and 59-60. Please note, the Medline reference cited herein is used as a definition only (to define what are encompassed within the neurodegenerative diseases), and not as a prior art.

Rejection-35 U.S.C. 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 42, 44-47, 49-56 and 58-60 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (US 2005/0271655 A1).

21. Lee et al teach SEQ ID NO: 7 which comprises the instant SEQ ID NO: 3. The reference teaches that a soluble Nogo receptor-1 polypeptide consisting essentially of a N-terminal domain (NT), 8 leucine rich repeat domains (LRR) and a LRR C-terminal domain (LRRCT) of Nogo receptor-1...a soluble Nogo receptor-1 polypeptide selected from the group consisting of: amino acid residues 26-344 of SEQ ID NO: 6; **amino acid residues 26-310 of SEQ ID NO: 7**; amino acid residues 26-344 of SEQ ID NO: 8; amino acid residues 26-310 of SEQ ID NO: 9; amino acid residues 27-344 of SEQ ID NO:8; and amino acid residues 27-310 of SEQ ID NO: 9 (see paragraph [0024]), meeting the limitation of claims 49 and 58. The reference teaches a method of

promoting survival of a neuron comprising contacting the neuron with an effective amount of a soluble Nogo receptor-1 polypeptide...the soluble Nogo receptor-1 polypeptide is a fusion protein, e.g., an Fc-fusion protein. In some embodiments, the neuron is in a mammal displaying signs of symptoms of, e.g., multiple sclerosis, ALS, Huntington's disease, Alzheimer's disease, Parkinson's disease...spinal cord injury (see paragraph [0021] and claim 64), meeting the limitations of claims 42-44, 47, 49-50, 52, 56, and 58-59. Furthermore, the reference teaches that dosage regimens may be adjusted to provide the optimum desired response, a single bolus may be administered…to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage unit (see paragraph [0140]. The reference teaches providing a soluble Nogo receptor-1 polypeptide at or near the site of the neurons (see paragraphs [0145] and [0151] and [0153]), meeting the limitation of claims 46 and 55. The reference teaches all of the active method steps of the instant claims. The reference teaches the same patient population, the same compound being administered, and the pharmaceutically active dosage. Therefore, the reference meets the limitation of claims 42-47, 49-50, 52-55 and 58-59. The reference teaches that dosage regimens may be adjusted to provide the optimum desired response (e.g., a therapeutic or prophylactic response)…In some embodiments a therapeutically effective dose range for Nogo receptor-1 antibodies or antigen-binding fragments there of is 0.1-4 mg/kg per day (see paragraph [0140]). Please note, the reference also teaches the nonelected species, instant SEQ ID NOS: 4, 5 and 6. The difference between the

reference and the instant claims is that the reference does not teach that the therapeutically effective amount is from 1 μg/kg to 10 mg/kg.

22. However, it would have been obvious to one of ordinary skill in the art to optimize the dosage range or concentration, according to the optimum desired response. One of ordinary skill in the art would have been motivated to do so and expect that optimum dosage range would at least provide better response. The MPEP states the following: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* In re Aller, *220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); In re Hoeschele, *406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or

molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). There is a motivation to optimize the dosage concentrations, since the normal desire of scientists or artisans want to improve upon what is already known, and the MPEP states that this *provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages*. There is a reasonable expectation of success, because routine optimization would at least arrive at the optimal dosage that is the most effective in treating the condition or disorders being treated. From the teachings of the reference, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention. Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Response to Applicant's Arguments

23. Applicant argues that "the Examiner has not established that the ordinary artisan reading Lee would predictably arrive at claims 42 and 52, as currently presented, which are drawn to methods of treating a disease, disorder, or condition comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits." Applicant argues that "Lee does not expressly or

inherently disclose the administration of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits." Applicant further argues that "there is nothing in Lee to suggest a relationship between Nogo receptor and Aβ peptide or its precursor protein (APP, amyloid precursor protein), as Lee is directed to, inter alia, the interaction between Nogo receptor and Nogo ligand."

24. Applicant's arguments have been fully considered but have not been found persuasive. The active method step of the instant claim 42 is "administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide." Claim 44 recites that the "disease, disorder or condition is Alzheimer's disease". The active method step of the instant claim 52 is "administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduction of plaque deposit." Claim 53 recites that the "disease, disorder or condition is Alzheimer's disease". Lee reference explicitly teaches the same active method steps of instant claims. Lee reference teaches a method of administering an effective amount of soluble Nogo receptor-1 polypeptide and Nogo receptor-1 polypeptide fusion protein (Fc-fusion protein) to a mammal displaying signs or symptoms of multiple sclerosis, ALS, Huntington's' disease, Alzheimer's disease, Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injuries and spinal cord injury (see paragraph [0021]). Furthermore, the reference explicitly claims the method of administering a soluble Nogo receptor-1 polypeptide to the mammal displaying signs or symptoms of MS, ALS, Huntington's disease, Alzheimer's disease,

Parkinson's disease, diabetic neuropathy, stroke, traumatic brain injuries or spinal cord injury (see claim 64). The Lee reference teaches the SEQ ID NO: 7 which comprises the instant SEQ ID NO: 3. The reference teaches that a soluble Nogo receptor-1 polypeptide consisting essentially of a N-terminal domain (NT), 8 leucine rich repeat domains (LRR) and a LRR C-terminal domain (LRRCT) of Nogo receptor-1...a soluble Nogo receptor-1 polypeptide selected from the group consisting of: amino acid residues 26-344 of SEQ ID NO: 6; **amino acid residues 26-310 of SEQ ID NO: 7**; amino acid residues 26-344 of SEQ ID NO: 8; amino acid residues 26-310 of SEQ ID NO: 9; amino acid residues 27-344 of SEQ ID NO:8; and amino acid residues 27-310 of SEQ ID NO: 9 (see paragraph [0024]). Lee reference explicitly teaches nine (9) diseases that the Nogo receptor-1 polypeptide and fusion proteins are administered to. Therefore, it would have been obvious to one of ordinary skill in the art to administer the Nogo receptor-1 protein to any one of the nine diseases disclosed and claimed. One of ordinary skill in the art would be motivated to optimize the dosage concentration, since Lee reference teaches that dosage regimens may be adjusted to provide the optimum desired response (e.g., a therapeutic or prophylactic response)…In some embodiments a therapeutically effective dose range for Nogo receptor-1 antibodies or antigen-binding fragments there of is 0.1-4 mg/kg per day (see paragraph [0140]). Furthermore, since the reference teaches the same active method steps (i.e., same compounds, the same dose and the same patient population), the reference administering Nogo receptor-1 polypeptide to the Alzheimer's patients would necessarily reduce levels of Aβ peptide or

reduce the plaque deposits. Therefore, the reference is *prima facie* obvious over the instant claims.

Obviousness Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

26. Claims 42, 44, 47, 49-50, 52-53, 56 and 58-59 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-9 of U.S. Patent No. 7,465,705. Although the conflicting claims are not identical, they are not patentably distinct from each other because if one of ordinary skill in the art practiced the claimed invention of instant claims, one would necessarily achieve the claimed invention of U.S. Patent No. '705, and vice versa.

27. Instant claims are drawn to a method for reducing the levels of Aβ peptide in a mammalian brain, comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide, wherein the NgR1 comprises a peptide selected from the group consisting of SEQ ID NO: 3 (amino acids 26 to 310 of human NgR1). The claims do not recite the patient population, therefore, administration of the polypeptide to anyone, *in vivo* and *in vitro* (brain cells) would necessarily reduce the levels of Aβ peptide.

28. The claims of U.S. Patent '705 is drawn to an isolated soluble Nogo receptor-1 polypeptide comprising amino acids 26-310 of SEQ ID NO: 7, fused to immunoglobulin Fc. Claims 7-9 are drawn to a method for inhibiting growth cone collapse of a neuron, the inhibition of neurite outgrowth or neurite sprouting in a neuron, and promoting survival of a neuron at risk or dying, comprising contacting the neuron with the soluble Nogo receptor-1 polypeptide of claim 1. The patient population is not recited in these claims. The Nogo-receptor-1 polypeptide comprising amino acids 26-310 of SEQ ID NO: 7 is the same as the instant SEQ ID NO: 3.

29. Therefore, if one ordinary skill in the art practiced the instant claims, one would necessarily achieve the claimed invention of U.S. Patent No. ‘705, and vice versa, since the patient population is not defined. Therefore, if the polypeptide of instant claims is administered to anyone, any brain tissue, cells, one would necessarily achieve the claimed invention of U.S. Patent No. ‘705, and vice versa.

Response to Applicant's Arguments

30. Applicant argues that "the methods of claims 7-9 of the '705 patent are directed to inhibiting growth cone collapse of a neuron, decreasing the inhibition of neurite outgrowth or neurite sprouting in a neuron, and promoting survival of a neuron at risk of dying. In contrast, the methods of the presently claimed invention are directed to methods of treating a disease, a disorder, or condition by reducing the levels of Aβ peptide in a mammalian brain or to methods of treating a disease, disorder, or condition associated with plaques of Aβ peptide in a mammalian brain…Thus, the claims of '705 patent do not render obvious the methods of the presently claimed invention."

31. Applicant's arguments have been fully considered but have not been found persuasive. The claims of patent '705 teaches the same active method steps of instant claims. Claims 7-9 of the patent '705 are drawn to a method for inhibiting growth cone collapse of a neuron, the inhibition of neurite outgrowth or neurite sprouting in a neuron, and promoting survival of a neuron at risk or dying, comprising contacting the neuron with the soluble Nogo receptor-1 polypeptide of claim 1. Since the claims are drawn to administering the Nogo receptor-1 polypeptide (the same peptide being claimed), this would inherently reduce the levels of Aβ peptide in a mammalian brain or reduce the plaque deposits in the mammalian brain. Therefore, the rejection is maintained.

Conclusion

32. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). No claim is allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Julie Ha/
Examiner, Art Unit 1654